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DOI: https://doi.org/10.1007/s00415-015-7777-5

J Neurol (2015) 262:2198–2199
DOI 10.1007/s00415-015-7777-5

PIONEERS IN NEUROLOGY

# Walter Rudolf Hess (1881–1973)

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Received: 27 April 2015 / Revised: 4 May 2015 / Accepted: 5 May 2015 / Published online: 19 May 2015


Walter Rudolf Hess (1881–1973) was born on March 17, 1881, in Frauenfeld (Switzerland) as the son of Gertrud Fischer and college physics professor Clemens Hess. Still a child, Hess was introduced to life sciences, helping his father to collect plants and butterflies and then taking part in his physics experiments. Stimulated by these early scientific experiences, Hess started studying medicine at the University of Lausanne in 1899. He pursued his medical studies at the Universities of Bern, Berlin, Kiel, and Zurich. While observing a vascular anomaly during a class on dissection, Hess speculated about a hemodynamic influence on the arterial system. Encouraged by anatomist Wilhelm Roux (1850–1924), this observation led to his first research article [1]. Hess kept a lifelong interest in hemodynamics.

Following his MD graduation from the University of Zurich in 1906, Hess became an assistant of the surgeon Conrad Brunner (1859–1927) in Munsterlingen. Realizing the clinical importance of the blood's composition, Hess designed, as autodidact, a device to measure blood viscosity, which was later used in the medical laboratories as "Hess viscosimeter" [2]. To pursue his scientific studies, Hess took a residency in ophthalmology under Otto Haab (1850–1931) at Zurich University in 1907. Here, he acquired the rigor and precision that would later serve him in his experimental research. During this time, he developed a new method to objectively quantify eye muscle deviations in diplopia, the "Hess screen" which is still in use today [3].

Upon return from a short training in venereology and neurology in Paris, Hess worked as a private ophthalmologist near Zurich from 1908 to 1912. Driven by his fascination for science, he accepted an assistant position proposed by Prof. Justus Gaule (1849–1939) at the Physiological Institute of the University of Zurich in 1912. One year later, Hess presented a vascular system model with optimal hemodynamics in his habilitation treatise [4], and was promoted to Privatdozent. After active duty in the Swiss Army Medical Corps during World War I, Hess joined the neurophysiologist Max Verworn (1863–1923) in Bonn, Germany. While working with Verworn, whose physiological concepts and synthetic approach proved essential for his further career, Hess acquired expertise in general animal physiology and continued his research on hemodynamics. In 1917, Hess became director of the Physiological Institute in Zurich. His first action was to reform teaching by introducing a course in experimental procedures.

Hess made major contributions to the field of neurophysiology, with a special focus on the diencephalon. Using electrical brain stimulation in freely moving cats, Hess produced a series of works that eventually, in 1949, led to the Nobel Prize in Physiology or Medicine "for the discovery of the functional organization of the diencephalon as a coordinating center of visceral function" (Fig. 1). Starting with the experimental investigation of the peripheral hemodynamics, Hess turned progressively to the central regulation of circulatory and respiratory functions. Following the pioneering work of Johann Karplus (1866–1936), Alois Kreidl (1864–1928), and Philip Bard (1898–1977), illustrating the association between autonomic nervous system and hypothalamus, Hess studied the diencephalic role in conveying sensory inputs to autonomic and extrapyramidal motor

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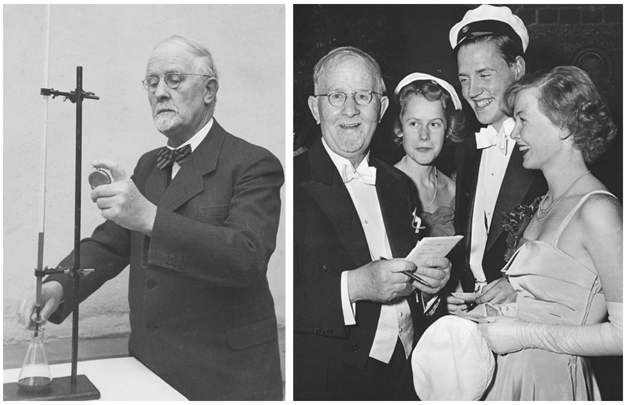

**Fig. 1** W. R. Hess demonstrates an experiment during a lecture in 1950 (*left*), and is celebrated for his Nobel Prize in 1949 by a delegation of students from Zurich (*right*)

outputs. Both a passionate technician and creative thinker, Hess successfully identified and stimulated the small and poorly myelinated fibers of the autonomic system using self-made tiny electrodes and a new stimulation technique ("interrupted direct-current (DC) stimulation") [5]. This new approach allowed him to create an atlas of the cat diencephalon based on serial histological sections.

Through his electrical exploration of the brain, Hess recognized the diencephalon, and particularly the hypothalamus, as the central integrator of autonomic functions. Hess described two anatomical zones: the "trophotropic" (parasympathetic) zone located in the anterior hypothalamus and the "ergotropic" (sympathetic) zone located in the posterior hypothalamus. Stimulating or lesioning these zones and nearby regions not only affected blood pressure, heart rate, and respiratory rate, but provoked somatomotor effects such as defense-like behavior, hunger, thirst, or defecation. These complex reactions reflected goal-directed and emotionally affected states and revealed the hypothalamus as a principal regulator of motivational and instinctive behaviors. In addition, Hess showed that the diencephalon contributes to the spatio-temporal coordination of head and body movements [6]. He emphasized the reciprocal relation between postural and goal-directed motor systems and proposed a concept of a proactive anticipatory control provided by posture, thereby challenging Sherrington's (1857–1952) conventional view of postural reflexes [7].

Hess is particularly famous for his studies on the sleeping cat. He observed various sleep-related autonomic changes and concluded that certain brain areas are active during sleep. Using electrical stimulation of the diencephalon and its surroundings [8–10], Hess found that "sleep-positive" and "sleep-negative" regions were able to induce both sleep and arousal. Although his son Rudolf M. Hess (1913–2007), who introduced electroencephalography in Switzerland, reproduced the results while recording characteristic sleep-EEG patterns in 1950, Hess' findings on electrically induced sleep remained controversial for many years. Other investigators were unable to replicate his observations, and there was no consensus on the neuroanatomical underpinnings of sleep regulation. These differences were likely due to methodological dissimilarities. Today, the central role of the diencephalon in sleep-wake regulation has been established by abundant data.

Since his early career, Hess questioned the popular theory of functionally independent nuclei, and his discovery of a dynamic equilibrium between autonomic and somatomotor changes provided supportive evidence of his concern. Eventually, linking physiology and behavior, Hess paid increasing attention to psychic functions and their impact on measurable neurophysiological features. Hess' work significantly advanced neurosciences, filling the gap between physiology and cognition and establishing the foundations for our knowledge about the organization of the central nervous system. Overall, Hess' extensive mapping of the diencephalic function represented a major contribution to neuroscience and paved the way to surgical treatments that can be offered today to patients with incapacitating motor and behavioral disorders.

After his retirement in 1951, Hess continued to work on his experimental findings before eventually moving to Ascona in 1967, where he died in August 1973 at the age of 92 years.

**Conflicts of interest** All authors declare that they have no conflict of interest.

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